IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

HOSPIRA, INC. and ORION CORPORATION, Plaintiffs, v. EUROHEATH INTERNATIONAL SARL and WEST-WARD PHARMACEUTICAL CORP., Defendants.	)	C.A. No. 14-487-GMS C.A. No. 14-1008-GMS

EUROHEALTH'S OPENING CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

This is a Hatch-Waxman case, brought by Hospira, Inc. and Orion Corporation (collectively, "Hospira" or "Plaintiffs") on the basis of Eurohealth International SARL and West-Ward Pharmaceutical Corp.'s (collectively, "Eurohealth") Abbreviated New Drug Applications to market generic versions of the drug product Precedex™, which contains dexmedetomidine hydrochloride as its active ingredient. Hospira asserts one patent in this litigation: U.S. Patent No. 6,716,867 ("the '867 patent"') (attached as Exhibit 1).

This is not the first venue in which the '867 patent has been adjudicated. In May 2012, following a multi-day trial in the District of New Jersey, Judge Cooper issued a final judgment, holding in relevant part that the claims of the '867 patent are invalid as obvious.[1] Hospira appealed, but while the appeal was pending, it settled with the defendants (Sandoz Inc. and Sandoz Canada Inc.). Pursuant to the parties' joint request, the New Jersey court then vacated the judgment,[2] leaving Hospira free to assert the previously-invalidated patent against additional parties, including Eurohealth.

At issue here are six claim terms, which are found (in italics) in the following representative claims:

> 1. A method of *sedating a patient* in an *intensive care unit*, which comprises administering to the patient an effective amount of *dexmedetomidine* or a pharmaceutically acceptable salt thereof, wherein the patient remains *arousable and orientated*.
>
> 8. The method according to claim 7, wherein the *loading dose* of dexmedetomidine is 0.2-2 μg/kg.

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[1] Exhibit 2, *Hospira, Inc., et al. v. Sandoz Inc., et al.*, No. 09-cv-04591, 2012 WL 1587688, at *34 (D.N.J. May 4, 2012) (hereinafter "*Sandoz*").

[2] Exhibit 3, *Hospira, Inc., et al. v. Sandoz Inc., et al.*, No. 09-cv-0491, 2014 WL 794589, at *1 (D.N.J. Feb. 27, 2014).

> 10. The method according to claim 7, wherein the *maintenance dose* of dexmedetomidine is 0.1-2.0 μg/kg/h.

As set forth in detail below, Eurohealth's proposed constructions find support in the claim language itself, the specification, and the prosecution history, whereas Hospira's proposed constructions do not. Indeed, in Hospira's prior suits, it proffered constructions of "intensive care unit" and "arousable and orientated" different than it proposes here, and that were in fact the same as or track language used in Eurohealth's current proposals.[3] However, having lost once on validity, Hospira now attempts to introduce limitations into these terms and the other disputed terms in an apparent effort to distance the '867 patent claims from the invalidating prior art relied upon by the New Jersey court. For the reasons discussed below, Hospira's litigation-driven proposals should be rejected, and Eurohealth's proposals should be adopted.

[3] For example, in litigations in the District of New Jersey and the Eastern District of Michigan, Hospira asserted that "arousable and orientated" meant "capable of being awakened and aware of one's environment"—which is precisely what Eurohealth proposes here. *See* Exhibit 4, Second Amended Joint Claim Construction and Prehearing Statement, *Sandoz*, No. 09-cv-04591 (D.N.J. May 25, 2011), D.I. 217-1 at 3; Exhibit 5, Joint Statement of Proposed Claim Constructions, *Hospira, Inc., et al. v. Caraco Pharm. Labs., Ltd. et al.,* Civ. No. 10-cv-14514 (E.D. Mich. Oct. 7, 2011), D.I. 26-1 at 1 (hereinafter "*Caraco*").

II. ARGUMENT

A. Based on the Claims and Specification, "Dexmedetomidine" Refers Only to the Free Base, and Does Not Include Pharmaceutically Acceptable Salts Thereof

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
1-12	dexmedetomidine	substantially pure, optically active dextrorotary stereoisomer of medetomidine, as the free base or pharmaceutically acceptable salt	substantially pure, optically active dextrorotary stereoisomer of medetomidine, as the free base

The parties dispute whether the claim term "dexmedetomidine" refers only to dexmedetomidine as the free base, or whether the term intrinsically includes all pharmaceutically acceptable salts as well. The intrinsic evidence easily resolves this question. The claims themselves and the specification clearly and repeatedly distinguish between dexmedetomidine and salts thereof.

"First and foremost, the analytical focus of claim construction must begin, and remain centered, on the language of the claims themselves." *ACTV, Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1088 (Fed. Cir. 2003). "[C]laims are to be interpreted with an eye toward giving effect to all terms in the claim" because a construction that leaves elements described in the claim "merely superfluous would render the scope of the patent ambiguous." *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006). The Federal Circuit has also emphasized that the specification "is the single best guide to the meaning of a disputed term." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (en banc). Accordingly, "claims must be read in view of the specification, of which they are a part." *Id.* at 1316 (citation omitted); *see also Reinshaw PLC v. Marposs Societa'per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998) ("The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.").

Here, the claims clearly distinguish between "dexmedetomidine" and "dexmedetomidine or a pharmaceutically acceptable salt thereof." For example, claims 1, 4, and 5 recite dexmedetomidine "or a pharmaceutically acceptable salt thereof," whereas claims 6, 8, and 10 switch to dexmedetomidine only:

> 1. A method of sedating a patient in an intensive care unit, which comprises administering to the patient an effective amount of ***dexmedetomidine or a pharmaceutically acceptable salt thereof***, wherein the patient remains arousable and orientated.
>
> 4. The method according to claim 1, wherein the ***dexmedetomidine or pharmaceutically acceptable salt thereof*** is administered in an amount to achieve a plasma concentration of 0.1-2 ng/ml.
>
> 5. The method according to claim 4, wherein the ***dexmedetomidine or pharmaceutically acceptable salt thereof*** is administered intravenously.
>
> 6. The method according to claim 5, wherein a loading dose and a maintenance dose of ***dexmedetomidine*** are administered.
>
> 7. The method according to claim 6, wherein the patient is a human.
>
> 8. The method according to claim 7, wherein the loading dose of ***dexmedetomidine*** is 0.2-2 μg/kg.
>
> 10. The method according to claim 7, wherein the maintenance dose of ***dexmedetomidine*** is 0.1-2.0 μg/kg/h.

Exhibit 1 ('867 patent) at col. 14, ll. 13-50. Thus the patentee knew how to distinguish between dexmedetomidine and its pharmaceutically acceptable salts, and Eurohealth's construction gives meaning to this difference. *See Pass & Seymour, Inc. v. Int'l Trade Comm'n*, 617 F.3d 1319, 1324 (Fed. Cir. 2010) (rejecting patentee's construction and noting that "[i]f [plaintiff] wanted its claim to read on devices [with certain limitations], then it could have written its claim" to do so). The patentee's decision to exclude "a pharmaceutically acceptable salt thereof" from claim 6-12 is a clear expression that those claims do not include salts. *See, e.g.*, *Viiv Healthcare UK Ltd. v. Lupin Ltd.*, 6 F.Supp.3d 461, 476 (D. Del. 2013) (refusing to construe "abacavir" to include salt

forms when other claims "manifestly recite derivatives of abacavir that would include the salt forms"), *aff'd*, 594 Fed. App'x 686 (Fed. Cir. 2015); *Source Vagabond Sys. Ltd. v. Hydrapak, Inc.*, 753 F.3d 1291, 1300 (Fed. Cir. 2014) ("[Plaintiff] had the ability to draft the claim that way but did not. It cannot correct that failure by adding words to otherwise unambiguous claim language.").

Further, the specification expressly defines "dexmedetomidine" without reference to salts, *i.e.*, as "(+)-(S)-4-[1-(2,3-dimethylphenyl) ethyl]-1H-imidazole," and provides the following chemical formula, which likewise lacks reference to salts:

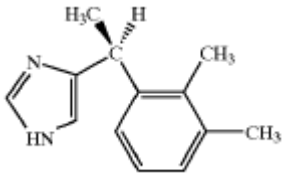

Exhibit 1 at col. 2, l. 66 – col. 3, l. 10. This distinction between dexmedetomidine and salts thereof is carried throughout the specification. To list just a few examples, at the beginning of the specification, the inventors stated: "The present invention relates to the use of dexmedetomidine **or** a pharmaceutically acceptable salt thereof in intensive care unit (ICU) sedation." *Id.* at col. 1, ll. 12-14 (emphasis added). In describing the allegedly inventive method, they again state: "[a]ccordingly, the present invention relates to a method of sedating a patient while in the ICU by administering dexmedetomidine **or** a pharmaceutically acceptable salt thereof." *Id.* at ll. 19-22 (emphasis added). Later, in the "Detailed Description of the Invention" section, the inventors stated: "[d]exmedetomidine **or** a pharmaceutically acceptable salt thereof can be administered perorally, transmucosally, transdermally, intravenously or intramuscularly." *Id.* at col. 5, ll. 5-7 (emphasis added). *C.f. SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1203 (Fed. Cir. 2013) (relying on the specification's consistent use of the

disjunctive terms "or'" and "as opposed to" to distinguish between a claimed and excluded method).

Hospira's proposed broadening construction of "dexmedetomidine" as including the free base plus pharmaceutically acceptable salts of dexmedetomidine is contrary to how the term is used in the claims, and to the specification's careful and repeated distinction between dexmedetomidine and salts thereof. Further, such a construction improperly renders the words "or a pharmaceutically acceptable salt thereof" in claims 1-5 superfluous. *See Becton Dickinson & Co. v. Tyco Healthcare Group, LP*, 616 F.3d 1249, 1257 (Fed. Cir. 2010) (refusing to adopt a claim construction that would render a claim limitation meaningless); *Bicon, Inc.*, 441 F.3d at 950 (stating that claims must be "interpreted with an eye toward giving effect to all terms in the claim."). Hospira's reliance on statements the applicant made during prosecution that "dexmedetomidine" includes salts should be rejected because prosecution statements cannot enlarge the scope of the claims beyond what the specification supports. *See, e.g., Biogen, Inc. v. Berlex Labs., Inc.*, 318 F.3d 1132, 1140 (Fed. Cir. 2003) ("[r]epresentations during prosecution cannot enlarge the content of the specification").

In view of the above, Eurohealth's proposed construction of dexmedetomidine should be adopted, as it is consistent with the claims and specification of the '867 patent, which repeatedly distinguish between dexmedetomidine and salts thereof.

B. Eurohealth's Construction of "Intensive Care Unit" is Consistent with the Specification and the Plain Meaning of the Term to a Person of Ordinary Skill in the Art, Whereas Hospira Seeks to Read in Narrowing Limitations

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
1-12	intensive care unit	any setting that provides care to critically ill patients, typically characterized by high nurse-to-patient ratios, continuous medical supervision, and intensive monitoring	any setting that provides intensive care, characterized by continuous medical supervision and intensive monitoring

The parties agree that "intensive care unit" refers to a setting that provides a particular kind of care, but they differ over exactly how to define the care provided in such a setting. Eurohealth's proposal tracks the express definition of the term in the specification and reflects the plain and ordinary meeting to a person of ordinary skill in the art.

The specification expressly defines "intensive care unit" as a physical setting, namely "any setting that provides intensive care." *See* Exhibit 1 at col. 1, ll. 17-18; col. 4, ll. 44-45. Eurohealth initially proposed this construction, and indeed, that is the construction Hospira itself stipulated to in its previous litigations.[4] However, during the meet and confer process leading to this brief, Hospira complained that Eurohealth's original proposal left unanswered what is meant by "intensive care."[5] Accordingly, in an effort to address Hospira's concerns and obviate the

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[4] Exhibit 4, Second Amended Joint Claim Construction and Prehearing Statement, *Sandoz*, No. 09-cv-04591 (May 25, 2011, D.N.J.), D.I. 217-1 at 3 (In the *Sandoz* litigation, Hospira and Sandoz agreed that "intensive care unit" means "any setting that provides intensive care"); *see also* Exhibit 5, Joint Statement of Proposed Claim Constructions, *Caraco*, No. 10-cv-14514 (E.D. Mich. Oct. 7, 2011), D.I. 26-1 at 1 (In the *Caraco* litigation Hospira argued that "intensive care unit" meant "any setting that provides intensive care").

[5] Hospira made this argument, despite previously telling the Eastern District of Michigan court that "intensive care" is not a claim term and does not need construction. Exhibit 6, Plaintiffs' Opening Claim Construction Memorandum, *Caraco*, No. 10-cv-14514 (E.D. Mich. Apr. 13, 2012), D.I. 51 at 8-9 ("'intensive care' is not a phrase that appears in the claims outside the context of 'intensive care unit' and therefore need not be construed").

need for briefing this term, Eurohealth specified that intensive care is characterized by continuous medical supervision and intensive monitoring.

This characterization is consistent with the specification, which for example discloses in Example 2 that the patients received monitoring of adverse events, vital signs, oxygen saturation, and concomitant medications, as well as cardiac monitoring and laboratory tests. *Id.* at col. 6, ll. 56-59. In Example 3, patients were continuously monitored, *e.g.*, they were observed and assessed for an additional 24 hours after cessation of dexmedetomidine. *Id.* at col. 8, ll. 21-23.

Identifying the features of "intensive care" as continuous medical supervision and intensive monitoring is also consistent with the plain and ordinary meaning of the term to a person of ordinary skill in the art. As Eurohealth's expert Dr. Daniel Talmor, Chairman of the Department of Anesthesia, Critical Care and Pain Medicine at Beth Israel Deaconess Medical Center and Professor of Anesthesiology at Harvard Medical School, explains, patients receiving intensive care would always be under continuous medical supervision and intensive monitoring. *See* Expert Declaration of Daniel Talmor, M.D., M.P.H., in Support of Eurohealth's Opening Claim Construction Brief ("Talmor Dec.") at ¶¶ 29-31. For example, Emergency Rooms, Post-Anesthesia Care Units, and Coronary Care Units, in addition to the physical area of a hospital designated as the "Intensive Care Unit" ("ICU"), are all settings that provide intensive care to patients. In these settings, patients often receive intensive monitoring, such as monitoring of heart rate, blood pressure, cardiac output, oxygen levels, body temperature, and respiration. *Id*. Patients receiving intensive care are also frequently subject to continuous medical supervision. *Id.* For example, a doctor is typically nearby at all times to address emergency patient needs.

Hospira's proposed construction suffers from several infirmities. First, it is unclear whether the language following the phrase "typically characterized by" is intended to limit the

claim scope. Second, whereas the claim term focuses on *where* the care is provide, Hospira seeks to import a limitation as to *whom* the care is provided by reading in the term "critically ill patients." During prosecution, Hospira amended the claims to limit them to a particular type of patient (a patient "in need of intensive care"), but ultimately abandoned the amendment in view of the Examiner's rejection.[6] The applicants thus replaced the words "in need of intensive care," which modified the patients, with the words "intensive care unit," which specified a location. *See* Exhibit 8, August 9, 2002 Amendment, JNT-PRECEDEX00371767-75, at 2 and 10 (emphasis added). Hospira is now attempting to reintroduce a limitation defining the type of patients through claim construction. But the law does not allow a patentee to regain through claim construction what it gave up during prosecution. *See, e.g.*, *Laryngeal Mask Co. v. Ambu A/S*, 618 F.3d 1367, 1372–73 (Fed. Cir. 2010) (rejecting the district court's reading of a limitation into the term and relying in part on evidence in the prosecution history that the applicant had previously amended claim to remove the limitation in question).

Further, as Dr. Talmor points out, intensive care is not limited to critically ill patients; it can also be provided to patients in unstable conditions in settings outside of the ICU proper. Talmor Dec. at ¶¶ 31, 33.

Finally, the additional requirement in Hospira's construction that intensive care be characterized by "high nurse–to-patient ratios" is not supported by the intrinsic evidence, and is not consistent with the characteristics of all intensive care settings outside of rooms denoted "intensive care units" in major hospitals. Talmor Dec. at ¶ 32.

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[6] Specifically, the Examiner rejected the amended claims as indefinite because ". . . 'in need of intensive care' is confusing. It is not clear that the patient is receiving care in an intensive care unit. Amending the claim to recite 'A method of sedating a patient who is receiving care in an intensive care unit . . .' would overcome this rejection if this is the intent of the applicants." Exhibit 7, February 11, 2002 Office Action, JNT-PRECEDEX00371760-62, at 2.

C. "Sedating a Patient [in an Intensive Care Unit]" Means Rendering a Patient Calm or Asleep, and Optionally Treating Conditions that Affect Patient Comfort

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
1-12	sedating a patient [in an intensive care unit]	rendering a patient calm and managing patient comfort [in any setting that provides care to critically ill patients, typically characterized by high nurse-to-patient ratios, continuous medical supervision, and intensive monitoring]	rendering a patient calm or asleep, and optionally treating conditions that affect patient comfort, [in any setting that provides intensive care, characterized by continuous medical supervision and intensive monitoring]

This term repeats "in an intensive care unit," which is addressed above. Accordingly, Eurohealth will focus here on the new words in the term, "sedating a patient." Eurohealth's construction differs from Hospira's in two ways: (1) it clarifies that sedating a patient includes rendering the patient calm *or* asleep; and (2) it clarifies that treating conditions that affect patient comfort (*e.g.*, treating pain or relieving anxiety) is an optional, not mandatory, component of sedating a patient.

Inclusion of the words "or asleep" in Eurohealth's construction is consistent with the claim language, specification, and the plain and ordinary meaning of the term "sedating." To start with, use of the word "arousable" elsewhere in the claims implies that some patients are asleep, so that they can be aroused. Indeed, both parties propose that "arousable and orientated" means, in relevant part, "capable of being ***awakened***." The patient must first be asleep before they can be "awakened."

Further, the specification discloses the Ramsay Sedation Scale for assessment of sedation levels in patients, which uses the term "asleep" in Scores 4 through 6. *See* Exhibit 1 at Figure 1. Several of the patent's examples disclose the sedation of patients with dexmedetomidine to achieve a Ramsay Sedation Scale score of 4. *See, e.g.*, *Id*. at col. 10, ll. 11-12 ("The patient's Ramsey [*sic*] Sedation Score was maintained at approximately 4"); *id*. at col. 10, ll. 44-45 ("The

Ramsey [*sic*] Sedation Score was maintained at approximately 4"); and *id*. at col. 11, ll. 54-55 ("While on dexmedetomidine and intubated, she had a Ramsey [*sic*] Sedation Score of 4."). Additionally, with respect to case study 13, the specification states that the desired level of sedation was easily achieved, and that the patient "remained calm and ***asleep*** when free of external stimuli." *Id.* at col. 12, ll. 46-47 (emphasis added). These examples are consistent with a person of ordinary skill in the art's understanding of sedation as rendering the patient calm or asleep. Talmor Dec. at ¶¶ 34-36.

As to whether addressing patient comfort is mandatory or optional, Eurohealth's proposal is again consistent with the specification. For example, the "Summary of the Invention" states that "the method for sedating a patient in the ICU encompasses all of the potential ICU uses of dexmedetomidine . . . including all potential uses from their activity as α2-agonists, *e.g*., their use as hypotensive agents, anxiolytics, analgesics, sedatives, and the like." Exhibit 1 at col. 3, ll. 44-49; *see also id*. at col. 4, ll. 38-43. The use of the language "potential uses," "*e.g*.," and "and the like" to offset the list of dexmedetomidine's uses indicates that the enumerated effects are optional, not mandatory as they are in Hospira's construction. This makes sense, because a person of ordinary skill in the art would understand that an agent used to sedate a patient in the ICU does not necessarily need to also treat conditions that affect patient comfort, such as pain. In some cases, ICU patients who require sedation are not in pain, *i.e*., substance overdose patients. Talmor Dec. at ¶¶ 37-38. In other cases, a separate agent is administered specifically for the treatment of pain and other conditions affecting patient comfort. *Id*.

This is apparent from the specification, where additional agents were administered to affect patient comfort. For example, in case study 1, the patient was sedated with dexmedetomidine, but required morphine, a painkiller. Exhibit 1 at col. 8, ll. 65-66. Thus, there

is no disclosure that the patient's comfort was necessarily managed by the dexmedetomidine. The same is true of case study 4 (patient required morphine, *see* col. 9, ll. 42-43); case study 5 (patient required morphine, *see* col. 9, ll. 63-65); case study 7 (patient required morphine, *see* col. 10, ll. 46-47); case study 8 (patient required morphine, *see* col. 10, l. 61 – col. 11, l. 19); and case study 13 (patient required morphine, *see* col. 12, ll. 50-52).

Finally, Eurohealth's proposal is consistent with the prosecution history. Specifically, the applicants told the Examiner: "When applicants refer to 'sedation' in the context of the invention, that term is used as defined in the specification at page 1, ll. 7-11; i.e., **sedation optionally together with treatment of conditions that affect patient comfort**." Exhibit 8, August 9, 2002 Amendment, JNT-PRECEDEX00371767-76, at 2 (emphasis added).

D. "Arousable and Orientated" Does Not Require that the Patient Interact With Others

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
1-12	arousable and orientated	capable of being awakened, aware of one's environment, and able to interact with others	capable of being awakened and aware of one's environment

The parties agree that "arousable and orientated" includes being capable of being awakened and aware of one's environment. The only dispute is whether this term *also* requires that the patient be "able to interact with others," as Hospira proposes.

Eurohealth's construction is correct because it gives a separate and unambiguous meaning to the distinct claim requirements "arousable" and "orientated," consistent with the separate use of those terms in the patent specification and the terms' plain and ordinary meanings. *See, e.g.*, Exhibit 1 at col. 1, ll. 37-41 (uses "arousable" without the term "orientated"); col. 2, ll. 17-20 (same); col. 6, ll. 28-29 (same); col. 8, ll. 49-52 (uses "oriented" without the term "arousable"; col. 12, ll. 10-11 (same); col. 12, ll. 28-30 (same); col. 13, l. 8 (same); col. 13, ll. 19-20; col. 13, ll. 42-44 (same). Eurohealth's proposed construction

accordingly assigns each of the words "arousable" and "orientated" its respective plain and ordinary meaning of "capable of being awakened" and "aware of one's surroundings."

Eurohealth is proffering the same construction Hospira proffered in two prior cases.[7] After seeing its patent held invalid in the *Sandoz* case, Hospira now attempts to insert a limitation that patients be "able to interact with others." This superfluous limitation does not match up with any words in the claims, which are adequately construed by the phrases "capable of being awakened" and "aware of one's surroundings," and is not required by the intrinsic record. It is axiomatic that while the claims in a patent are to be construed "in light of the specification," the court may not "import[] limitations from the specification into the claim." *Ericsson, Inc. v. D-Link Systems, Inc*., 773 F.3d 1201, 1218 (Fed. Cir. 2014) (citing *Phillips*, 415 F. 3d at 1316, 1323); *Alloc, Inc. v. Int'l Trade Comm'n*, 342 F.3d 1361, 1370 (Fed. Cir. 2003).

This is not a case in which the "specification read as a whole suggests that the very character of the invention requires the limitation be a part of every embodiment." *C.f. Alloc,* 342 F.3d at 1370. The '867 patent discloses case studies from a Phase III clinical trial using dexmedetomidine for ICU sedation. Exhibit 1 at col. 7, ll. 44-56; col. 8, ll. 48-52. The patients' level of sedation is described with reference to the Ramsay Sedation Scale, which assesses a patient's level of wakefulness based on progressive loss of responsiveness to stimuli ranging from auditory to deep painful stimuli. *See id*. at Fig. 1; col. 4, ll. 15-20. Several patients were

[7] Exhibit 4, Second Amended Joint Claim Construction and Pre-Hearing Statement, Sandoz, No. 09-cv-04591 (D.N.J. May 25, 2011), D.I. 217-1 at 3 (In the *Sandoz* litigation Hospira and Sandoz agreed that "arousable and orientated" meant "capable of being awakened and aware of one's environment"); Exhibit 5, Joint Statement of Proposed Claim Constructions, *Caraco*, No. 10-cv-14514 (E.D. Mich. Oct. 7, 2011), D.I. 26-1 at 1 (In the *Caraco* litigation Hospira argued that "arousable and orientated" meant "capable of being awakened and aware of one's environment").

reported to be asleep, and a patient who is asleep is unable to interact with anyone. *See, e.g.*, *id*. at col. 9, ll. 28-31 ("His Ramsay Sedation Score was 6 during the first hour (baseline score, *i.e.*, the patient was fully anaesthetized after surgery), then decreased to 4 and subsequently reached 3."); *id*. at col. 10, ll. 11-12 ("The patient's Ramsey [*sic*] Sedation Score was maintained at approximately 4."); *id*. at col. 10, ll. 44-45 ("The Ramsey [*sic*] Sedation Score was maintained at approximately 4"); *id.* at col. 11, ll. 54-57 ("While on dexmedetomidine and intubated, she had a Ramsey [*sic*] Sedation Score of 4. She was calm, easily arousable, and well-oriented."); *see also* Talmor Dec. at ¶ 41.

Other patients were described as calm and well-oriented, but there is no mention that they were able to interact with anyone. *See id*. at col. 12, ll. 10-11 ("He remained calm and quiet, yet well oriented."); *id*. at col. 12, ll. 28-31 ("During her postoperative course, the patient was calm, had no fear or apprehension, and was well oriented even though she had a little amnesia."). Accordingly, there is no basis to read in the superfluous limitation of "able to interact with others."

Finally, a person of ordinary skill in the art would not understand the term "arousable and orientated" to require that the patient "interact" with others in all situations. Talmor Dec. at ¶ 40. As Dr. Talmor explains, patients who are sedated may be capable of being awakened and aware of their surroundings, and yet be incapable of speaking coherently or understanding instructions from others. This is true, for example, with patients who are recovering from a substance overdose or suffering from certain types of brain injuries. *Id.*

For the above reasons, Hospira's additional proposed limitation should be rejected, and Eurohealth's proposal should be adopted.

E. "Loading Dose" Should Be Construed To Mean "Dose Administered To Achieve A Target Concentration"

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
6-12	loading dose	a dose that may be given at the onset of therapy with the aim of achieving the target concentration rapidly and that is distinct from, and comparatively larger than, its associated maintenance dose	dose administered to achieve a target concentration

Eurohealth's proposal that "loading dose" be construed to mean "dose administered to achieve a target concentration" is straightforward and consistent with the specification. It appears that the parties do not dispute that a loading dose is administered to "achieve a target concentration," as both sides' proposals include this concept. Indeed this is consistent with the specification, which provides a target plasma concentration range of dexmedetomidine that is expected to provide sedation in the ICU patient population. Exhibit 1 at col. 5, ll. 14-19. The specification explains that the target concentrations can be achieved by intravenous administration, using a bolus dose—which is an example of a loading dose—and continuing it by a steady maintenance infusion. *Id.* at col. 5, ll. 19-21.

Thus the core of the dispute is whether Hospira is correct that numerous additional limitations should be read into this term, including a dose that "may" be given at the onset of therapy; with the aim of achieving the target concentration "rapidly;" that is distinct from and "comparatively larger than," its associated maintenance dose. First, the limitation that the loading dose "may" be given at the onset of therapy is ambiguous—is what follows a requirement or not? Second, Hospira's attempt to read in a subjective timing limitation (*i.e.*, that the target concentration be achieved "rapidly") is inconsistent with the plain language of the claims. For example, claim 9 limits the administration of the loading dose to "about 10 minutes," whereas claims 6-8 and 10-12 contain no time limitation at all. Hospira's proposal

would thus introduce a vague and undefined time limitation into all of these claims, even though claims 6-8 and 10-12 were expressly written to be devoid of a time limitation. Reading "rapidly" into the claims is also inconsistent with the specification, which nowhere uses the term "rapidly" in conjunction with administration of a loading dose. To the contrary, the specification describes administration of the loading dose to achieve a target plasma concentration "in about 10 minutes *or slower*," and states that "[t]he time period for administering dexmedetomidine or a pharmaceutically acceptable salt thereof depends on the . . . desired duration of use." *See* Exhibit 1 at col. 5, ll. 25, 28-30 (emphasis added).

Similarly, Hospira's proposed requirement that the loading dose be "comparatively larger than" the associated maintenance dose is contrary to the claim language and is not required by the specification. Claims 8-12 recite overlapping ranges for loading and maintenance doses: compare claim 8 (loading dose as small as 0.2 μg/kg) with claim 10 (maintenance dose as large as 2.0 μg/kg/hr). *Source Vagabond Sys.*, 753 F.3d at 1299-1300 (rejecting a construction that essentially "added words to the actual claim language"). The "Detailed Description of the Invention" also recites overlapping ranges for loading and maintenance doses. *Id*. at col. 5, ll. 21-28 ("For example, the dose range for the bolus to achieve the aforementioned plasma concentration range in a human is about 0.2-2 μg/kg . . . to be administered in about 10 minutes or slower, followed by a maintenance dose of about 0.1-2.0 μg/kg/h . . . ."). A requirement that the loading dose be greater than the maintenance dose is also inconsistent with a case study in Example 3, wherein the loading dose was smaller than the maintenance dose. *Id.* at col. 11, ll. 6-10 ("A dexmedetomidine loading dose (0.4 μg/kg/h) was administered with propofol 20 mg at approximately 25 minutes after arrival in the ICU and was followed by infusions of dexmedetomidine 0.7 μg/kg/h and propofol 4 mg/kg/h."). Thus Hospira's attempt to read in

numerous limitations, which find no support in—and in fact are contrary to—the claims and specification, should be rejected. *See, e.g.*, *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1305 (Fed. Cir. 2007) ("We normally do not interpret claim terms in a way that excludes disclosed examples in the specification.").

Accordingly, the term "loading dose" should be construed to mean "dose administered to achieve a target concentration."

F. "Maintenance Dose" Should Be Construed to Mean "Dose Administered to Maintain a Target Concentration or Desired Effect," and Hospira's Extraneous Limitations Should be Rejected

Claims	Term	Hospira's Proposal	Eurohealth's Proposal
6-12	maintenance dose	a dose given as a continuous infusion that may be titrated in order to maintain the desired effect	dose administered to maintain a target concentration or desired effect

Like its proposal for "loading dose," Eurohealth's proposed construction of "maintenance dose" is straightforward and consistent with the specification. In contrast, Hospira's construction attempts to introduce additional, unnecessary limitations into the claims, including 1) requiring that the maintenance dose be "given as a continuous infusion," and 2) restricting the purpose of the maintenance dose to maintaining "the desired effect."

It appears that the parties do not dispute that a maintenance dose is administered to maintain a "desired effect," as both sides' proposals include this concept. Thus the question becomes whether a maintenance dose can also be administered to maintain "a target concentration," as per Eurohealth's proposal. It is clear from the specification that a maintenance dose can be administered to maintain either a target concentration or a desired effect. As noted above, the specification describes using a maintenance infusion to maintain a target plasma concentration. *See* Exhibit 1 at col. 5, ll. 19-21 ("These plasma concentrations can be achieved by intravenous administration by using a bolus dose and continuing it by a steady

maintenance infusion."). The specification also describes administering a maintenance dose to maintain a specific Ramsay Sedation Scale score. *See, e.g.*, *id*. at col 6, ll. 1-5 (discussing adjusting the maintenance infusion rate to achieve and maintain a Ramsay Sedation Score level of 3 or higher); col. 8, ll. 2-5 (same). Accordingly, Eurohealth's proposal of "dose administered to maintain a target concentration or desired effect" is consistent with the specification, whereas Hospira's proposal of restricting the purpose of the maintenance dose to maintaining "the desired effect" is too narrow because it would exclude embodiments disclosed in the specification. *See Verizon Servs. Corp.*, 503 F.3d at 1305.

Hospira's construction is incorrect for additional reasons. First, as discussed above with respect to "loading dose," the limitation that the maintenance dose "may" be titrated is ambiguous—is this a requirement or not? Second, Hospira's proposal requires "a continuous infusion," which is not inherent in the plain meaning of the term "maintenance dose." Indeed, the concept of maintenance dose applies across dosage forms. The inventors purported to broadly define the invention as including multiple dosage forms, such as peroral, transmucosal, transdermal, intravenous, and intramuscular administration, Exhibit 1 at col. 5, ll. 5-7, yet a "continuous infusion" is not applicable to all of these forms (such as solid dosage forms). Moreover, while the specification does refer to "infusion," it does not disclaim the use of other administration methods, or infusion techniques other than "continuous infusion" (*e.g.*, intermittent infusion). *See Phillips*, 415 F.3d at 1323 (holding that a court may not "import[] limitations from the specification into the claim"); *see also In re Papst*, 778 F.3d 1255, 1267 (Fed. Cir. 2015) (the mere "absence of something in the written description" "does not suggest a disclaimer of any sort").

Accordingly, Hospira's attempt to read in numerous limitations should be rejected, and the term "maintenance dose" should be construed in a manner consistent with the '867 patent specification to mean "dose administered to maintain a target concentration or desired effect."

III. CONCLUSION

For all of the above reasons, the Court should adopt Eurohealth's proffered constructions of the disputed claim terms.

Respectfully submitted,

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